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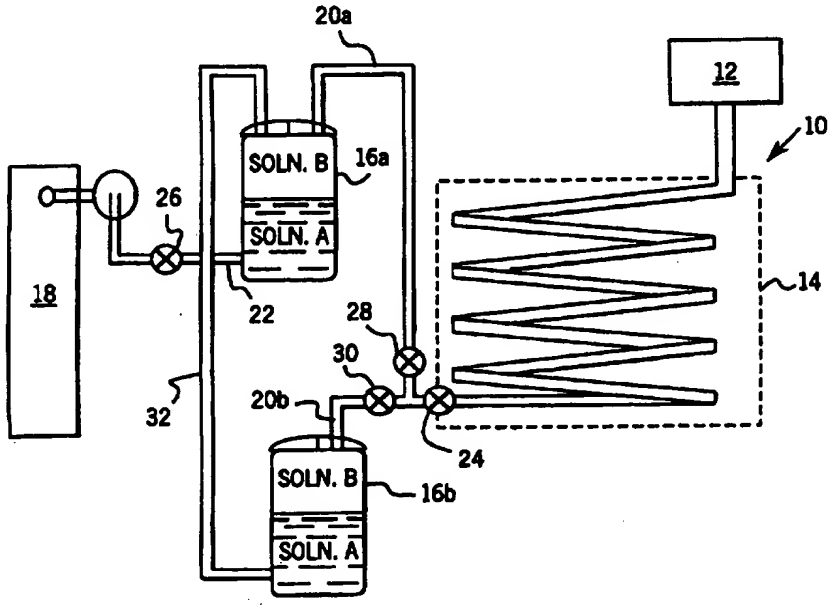

(57) Abstract

A method and system for sterilizing heat sensitive drugs which prevent degradation of the drug from heat and its associated by-products where the method includes providing separate relatively less heat sensitive component solutions of the drug for independent heat sterilization and then transferring the sterilized component solutions to a holding tank where they are mixed to form a final solution constituting the desired drug thereby avoiding heating of the final solution or drug and its possible degradation.

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METHOD AND SYSTEM FOR STERILIZING HEAT SENSITIVE DRUGS

Technical Field Of The Invention

The present invention relates generally to a method and system for sterilizing heat sensitive drugs which are formed by combining separate relatively less heat sensitive component solutions, where the separate component solutions are heat sterilized independently, and thereafter mixed in a holding tank to form a final solution comprising the drug while avoiding heat degradation of the drug which typically occurs when the drug is heat sterilized after mixing the component solutions.

Background Of The Invention

Sterilization of parenteral solutions or drugs typically is provided before packaging by an in-line sterilizer system which elevates the solution to a desired temperature. An example of such a system is disclosed in co-pending U.S. Application Serial No. 08/332,006, filed concurrently herewith, on October 31, 1994, entitled "Solution Sterilization System and Method of Operation" which is assigned to the assignee of the present application and is hereby incorporated by reference.

Some solutions, however, are mixed solutions of essentially two separate drugs, neither of which is particularly heat sensitive alone, but when combined provide a final solution or drug which is more susceptible to heat degradation and degradation byproducts.

Existing sterilization systems attempt to minimize drug degradation by rapidly heating and then cooling the mixed final solution or drug. Such systems, with various drugs and are not completely effective in reducing degradation and the associated by-products. It therefore would be desirable to provide a method and system for independently sterilizing the relatively less

heat sensitive component solutions of a drug prior to mixing of the component solutions to form the final solution comprising the drug to minimize if not eliminate any degradation problems.

Summary Of The Invention

The present invention provides a method and system for heat sterilizing a drug which minimizes or eliminates heat degradation and associated by-products of the drug, particularly of a mixed solution of essentially two separate relatively less heat sensitive solutions or drugs. The system minimizes heat degradation by separately sterilizing the relatively less heat sensitive solutions and then later combining the solutions to form the final solution.

In accordance with a first disclosed embodiment, the present sterilization system includes a first arrangement for supplying a first relatively less heat sensitive solution from an associated source and a heat sterilizing apparatus having one or more heat-exchangers for elevating the temperature and subsequently cooling the first solution. The system further includes a sterilized solution holding tank including a mixer therein which receives the first sterilized solution from the heat-exchangers.

A second arrangement is also provided for supplying a second relatively less heat sensitive solution from an associated source to the heat sterilizing apparatus for elevating the temperature and subsequently cooling the second solution. The second solution is received within the sterilized solution holding tank and mixed with the first solution to form the final mixed solution.

The heat sterilizing apparatus disclosed in the above-referenced co-pending application is preferably used to sterilize and transfer both the first and second solutions to the holding tank. In such a

situation, the apparatus would preferably be purged and cleaned between solutions as described in that co-pending application.

In accordance with a second disclosed embodiment, the present sterilization system includes first and second sterilized solution holding tanks for receiving the first and second solutions, respectively, from the heat sterilizing apparatus. The first and second holding tanks are interconnected to thereafter enable mixing in at least one of the holding tanks to form the final mixed solution.

Numerous other advantages and features of t:he present invention will become readily apparent from t:he following description of the invention, the claims and the accompanying drawings.

Brief Description Of The Drawings

FIGURE 1 is a schematic view of a first embodiment of a solution sterilization system according to the present invention which utilizes a single holding and mixing tank; and

FIGURE 2 is a schematic view of a second embodiment of a solution sterilization system according to the present invention which utilizes at least two holding and mixing tanks.

Description Of The Preferred Embodiments

While the present invention is susceptible of embodiment in many different forms, the specification and the accompanying drawings specifically disclose one or more forms as examples of the invention. The invention is not intended to be limited to the embodiments described, the scope of the invention being pointed out in the appended claims.

For ease of description, the method and system of this invention is described in the normal, upright, operating position and terms such as upper, lower,

horizontal etc. are utilized with reference to this position. It will be understood, however, that the apparatus of this invention may be manufactured, stored, transported and sold in an orientation other than the position described.

Some of the figures illustrating the embodiments of the system of the present invention show conventional components, structural details and mechanical elements that will be recognized by one skilled in the art. The detailed descriptions of such elements, however, are not necessary to an understanding of the invention and, accordingly, are not presented herein.

As FIGURE 1 illustrates, the present invention provides a system 10 for sterilizing a solution, preferably relatively heat sensitive parenteral solutions such as intravenous drugs. The system 10, however, may also be used to process drugs which are not heat sensitive as well as human and animal consumables.

In the present invention, the system 10 utilizes a novel solution sterilization method which minimizes if not eliminates heat degradation of the solution being processed by separately processing the relatively less heat sensitive component solutions which make up the final solution or drug when mixed. Thus, the prior art problem of heat degradation and associated by-products is avoided in the present invention thereby reducing waste of expensive pharmaceuticals.

The solution sterilization system 10 of the present invention generally includes a supply arrangement 12, including a pump (not illustrated), for supplying a solution to the system 10 from an associated product source. Although only one supply arrangement 12 is illustrated, it is to be understood that a number of different supply arrangements 12 can be utilized if desired, each preferably providing a different solution to the system 10.

The system 10 further includes a heat sterilization apparatus, such as an in-line sterilization system 14, illustrated in dotted lines, which includes one or more heat-exchangers for elevating the temperature of the solution for effecting sterilization and then cooling the solution. The sterilization system 14 can vary from the illustrated system so long as it provides sterilization of the solution as described herein.

A sterile solution holding tank 16 also is included as part of the system 10 having a mixing device therein (not illustrated). Finally, a filling apparatus 18 is included with the system 10 for providing the final mixed solution into individual packages, such as bags, vials or any similar container.

Suitable piping or conduits are used to connect the elements 12, 14, 16 and 18 of the system 10 so that the elements are in fluid communication with each other. Herein, these pipes or conduits will be referred to as "lines." Suitable valves also are provided in the system 10 along the lines to selectively start or stop the flow of solution.

Initially, the general elements of the system 10 will be described. Additional features, advantages and elements will be described in reference to the process for using the sterilization system 10.

The supply arrangement 12 pumps a solution into the system 10 from a source (not illustrated) so that sterilization of a desired solution can be effected. The solution from the supply arrangement 12 can be processed, such as by filtration or other method to at least minimize the bioburden, i.e., naturally occurring bacteria, in the solution.

The supply arrangement 12 is downstream of the source and in fluid communication with the source. The supply arrangement 12 may include a standard pump for pumping the solution from the source to the

sterilization system 14.

The sterilization system 14 is upstream of and in fluid communication with the holding tank 16 and downstream of and in fluid communication with the supply arrangement 12 and the solution source. The sterilization system 14 heat sterilizes the solution. The sterile holding tank 16 is used to accumulate and/or temporarily store solution sterilized by the sterilization system 14 and preferably is positioned between the sterilization system 14 and the filling apparatus 18. To assist in mixing solutions within the holding tank 16 as described below, the holding tank 16 includes an input line 20 positioned near a top of the holding tank 16 and an outlet line 22 positioned near the bottom of the holding tank 16.

A first valve 24 controls flow of solution between the sterilization system 14 and the holding tank 16 and a second valve 26 controls flow of solution between the holding tank 16 and the filling apparatus 18.

Suitable automatic programmable logic controls (not illustrated) are used to sequence and control the valves, pumps and other components of the system. The elements of the system 10 are coupled to the logic controls by suitable circuitry. The heat-exchangers within the sterilization system 14 are monitored by suitable thermocouples (not illustrated). Flow rate in the lines is monitored by one or more flow meters (not illustrated).

Having described the general elements of the system 10, the process for using the system 10 will now be described. Additional advantages and features of the general elements will become clear herein in reference to the process for using the system 10.

Before use, the system 10 preferably is steam sterilized and prepared for sterilization. The sterilization system 14 receives a first relatively less

heat sensitive solution, solution "A", from the supply arrangement 12 and elevates the temperature of the first solution to effect sterilization. In a current embodiment, solution is cooled immediately after sterilization.

After the first solution passes through the sterilization system 14, the solution passes through the open first valve 24 and enters into the holding tank 16 where it is temporarily stored. After a prescribed amount of first solution is sterilized and fed into the holding tank 16, the flow of solution is stopped, preferably by closing the first valve 24 and shutting down the sterilization system 14.

The sterilization system 14 then is purged to remove the first solution therefrom and prepared for sterilization of a second relatively less heat sensitive solution, solution "B", to be mixed with the first solution in the holding tank 16 and provide the final solution or desired drug. If desired, after purging the sterilization system 14 and before initiating sterilization of the second solution, the sterilization system 14 can be cleaned with rinse water, such as distilled water or the like, and then sterilized with high quality steam.

The sterilization system 14 receives the second solution from the supply arrangement 12 which is connected to a supply of second solution (not illustrated) and elevates the temperature of the second solution to effect sterilization. In a current embodiment, the solution is cooled immediately after sterilization. After passing through the sterilization system 14, the second solution flows through the open first valve 24 and into the holding tank 16 for mixing with the second solution.

After a prescribed amount of second solution is fed into the holding tank 16, the flow of second solution is stopped again by closing the first valve 24

and shutting down the sterilization system 14. A mixing device then is activated to provide proper mixing of the first and second solutions within the holding tank 16.

Once the proper mixing is achieved, the second valve 26 is opened and the final sterilized solution, comprised of both the first and second sterilized solutions, is pumped to the filling apparatus 18 for providing the final solution in appropriate containers.

It is to be noted that although the present embodiment has been described for mixing two solutions to obtain a final solution or drug, the system 10 can be utilized to individually sterilize a plurality of solutions for mixing in the holding tank 16 to form the desired final solution. When using more than two solutions, the system 10 is preferably purged of existing solution, rinsed and steam sterilized between solutions as described above.

FIGURE 2 illustrates another embodiment of the present invention where similar elements are identified by the same reference numerals as in the embodiment of FIGURE 1. In this embodiment, two holding tanks 16a and 16b are supplied with the first and second solutions respectively, along lines 20a and 20b and hold the first and second solutions prior to mixing. To provide the flow of solution to the holding tanks 16a and 16b, valves 28 and 30 are included.

After the first and second solutions are sterilized, the second solution, solution "B", is transferred from holding tank 16b to holding tank 16a through line 32 for mixing. The remaining elements and operation of this embodiment are substantially the same as in the embodiment of FIGURE 1.

From the foregoing, it will be observed that numerous modifications and variations can be effected without departing from the true spirit and scope of the novel concept of the present invention. It is to be understood that no limitation with respect to the

specific embodiments is intended or should be inferred. The disclosure is intended to cover by the appended claims all such modifications as fall within the scope of the claims.

What is Claimed Is:

1. A method of sterilizing a heat sensitive drug comprising a plurality of component solutions, said method comprising the steps of:

providing a first component solution;

providing a means for heat sterilizing;

placing said first component solution in said means for heat sterilizing;

heat sterilizing said first component solution using said means for heat sterilizing;

providing a first holding tank;

transferring said first component solution from said means for heat sterilizing to said first holding tank;

providing a second component solution;

placing said second component solution in said means for heat sterilizing;

heat sterilizing said second component solution using said means for heat sterilizing;

transferring said second component solution to said first holding tank;

providing a means for mixing said first and second component solutions; and

mixing said first and second component solutions within said first holding tank using said means for mixing to form a final solution.

2. A method as defined in claim 1, wherein said method further comprises the steps of providing a second holding tank, transferring said second component solution from said means for heat sterilizing to said second holding tank, and transferring said second component solution from said second holding tank to said first holding tank.

3. A method as defined in claim 1, wherein said method further comprises purging said means for heat sterilizing after transferring said first component

solution from said means for heat sterilizing to said first holding tank and prior to placing said second component solution in said means for heat sterilizing.

4. A system for sterilizing a heat sensitive pharmaceutical, said system comprising:

first supply means for supplying a first component solution;

second supply means for supplying a second component solution;

means for sterilizing said first and second component solutions, said means for sterilizing fluidly connected to said first and second supply means at a position downstream said first and second supply means;

a first holding tank for containing said first and second component solutions therein, said first holding tank fluidly connected to said means for sterilizing at a position downstream said means for sterilizing; and

means for mixing said first and second component solutions within said first holding tank, whereby said means for mixing mixes said first and second component solutions to form a final solution.

5. A sterilization system as defined in claim 4, wherein said system further comprises a second holding tank fluidly connected to said means for sterilizing at a position downstream said means for sterilizing and fluidly connected to first holding tank and means for transferring said first and second component solutions between said first and second holding tanks whereby said first and second component solutions can be mixed within at least one of said first and second holding tanks.

6. A sterilization system as defined in claim 4, wherein said system further comprises means for filling a container with said final solution, said means for filling fluidly connected to said first holding tank at a position downstream said first holding tank.

7. A method for heat sterilizing a pharmaceutical product, said method comprising:

providing a first component solution having a first heat sensitivity;

providing a means for heat sterilizing a solution;

placing said first component solution in said means for heat sterilizing;

heat sterilizing said first component solution using said means for heat sterilizing;

providing a holding tank;

transferring said first component solution from said means for heat sterilizing to said holding tank;

purging said means for heat sterilizing after transferring said first component solution from said means for heat sterilizing to said holding tank;

providing a second component solution having a second heat sensitivity;

placing said second component solution in said means for heat sterilizing after purging said means for heat sterilizing;

heat sterilizing said second component solution using said means for heat sterilizing;

transferring said second component solution to said holding tank;

mixing said first and second component solutions within said holding tank and forming a pharmaceutical product having a third heat sensitivity greater than said first and second heat sensitivities.

8. A method for heat sterilizing a pharmaceutical product in accordance with Claim 7, said method further comprising the steps of sterilizing said means for heat sterilizing prior to placing said first component solution in said means for heat sterilizing, and sterilizing said means for heat sterilizing prior to placing said second component solution in said means for heat sterilizing.

FIG. 1

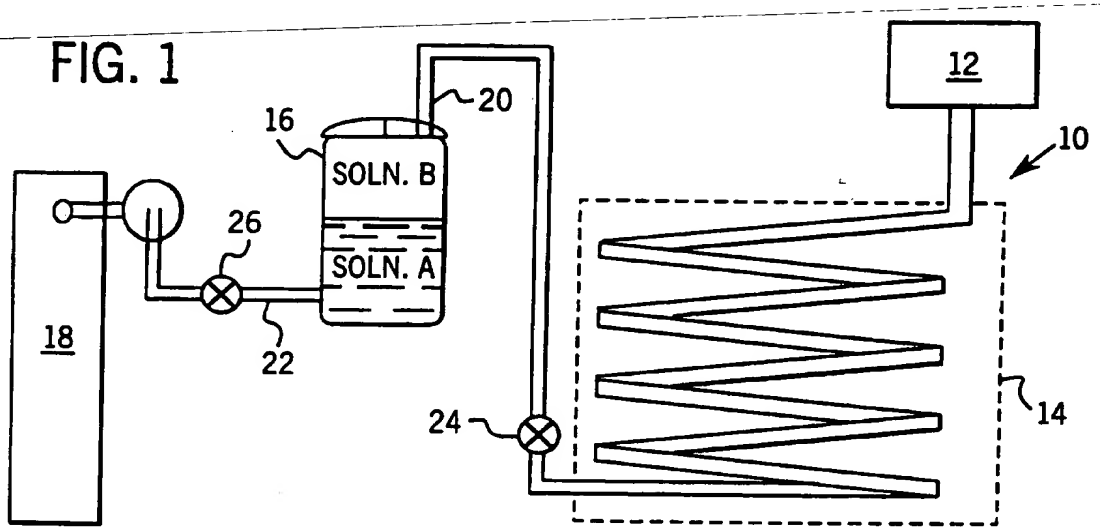
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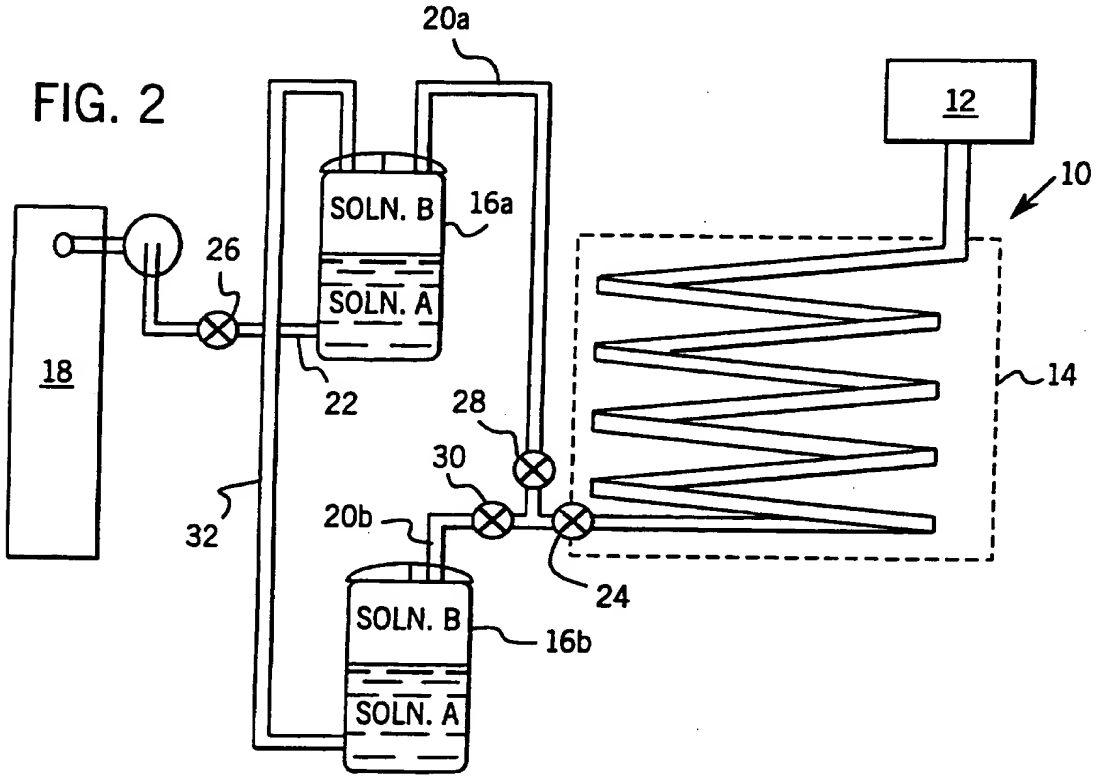
FIG. 2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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61L2/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 428 009 (GAMBRO) 22 May 1991	

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